

# Breast Cancer and Social Interactions: Identifying Multiple Environments that Regulate Gene Expression



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**The University of Chicago**

**Supported by P50-ES012382**





**Cancer Risk Clinic**

**Institute for  
Mind and Biology**



**University of Ibadan**

## **Center for Interdisciplinary Health Disparities Research**

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**Funmi Olopade, MD**  
**Thomas Krausz, MD**

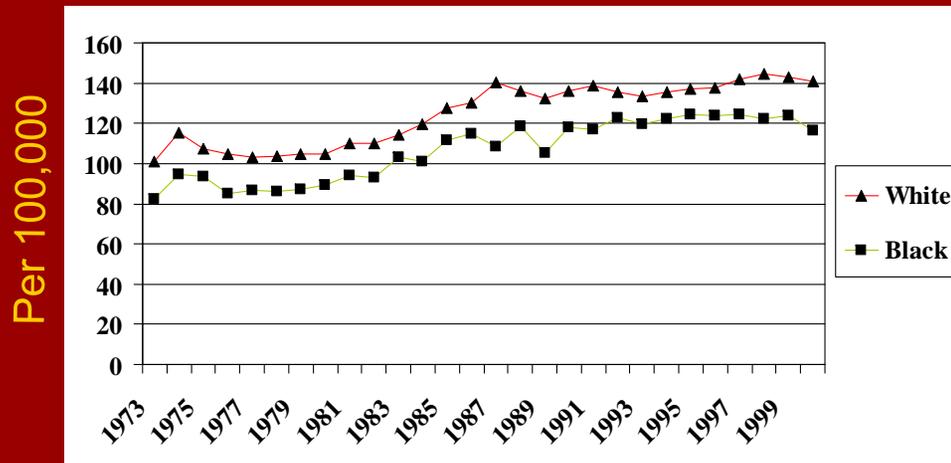
**School of Soc. Serv. Admin.**  
**Department of Psychology**  
**Department of Medicine**  
**Department of Medicine**  
**Department of Pathology**

## **CIHDR Central Research Question**

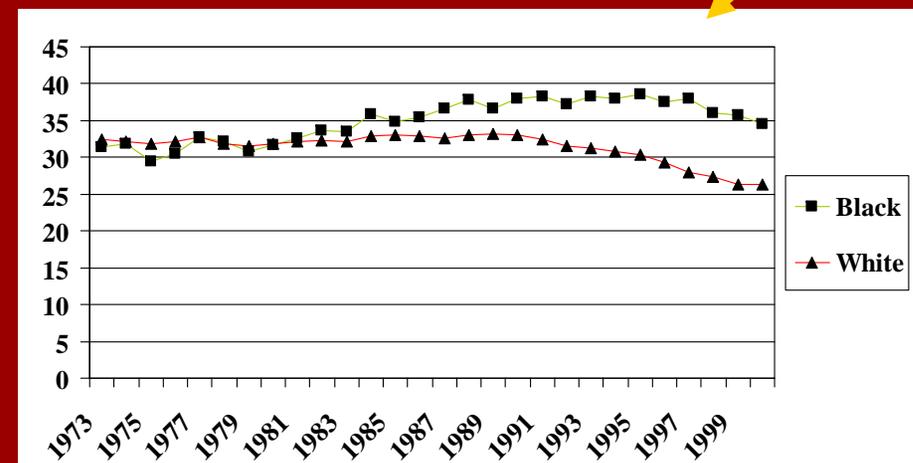
**How do factors in women's social environments contribute to the African American and white disparity in breast cancer mortality in the U.S.?**

# Black and White Age-Adjusted Breast Cancer Statistics, 1975-2000

## Incidence



## Mortality



Black women 37% higher

SEER Cancer Statistics Review, 1975-2000

## Why the Worse Outcome?

# Mutually Informative Multi-Level and Multi-Modal Approach

Projects 1 and 4

Projects 2 and 3

Olopade  
Gehlert

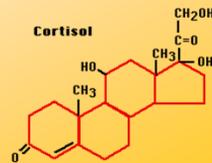
McClintock  
Conzen



genes



hormones



psychological  
state

behavior  
patterns

social  
circum-  
stances

(social  
isolation,  
social  
support)

housing

environ-  
mental  
exposure

community/  
neighbor-  
hood

(crime,  
collective  
efficacy,  
social  
ecology)

# Total Tumor Burden: 17 Months

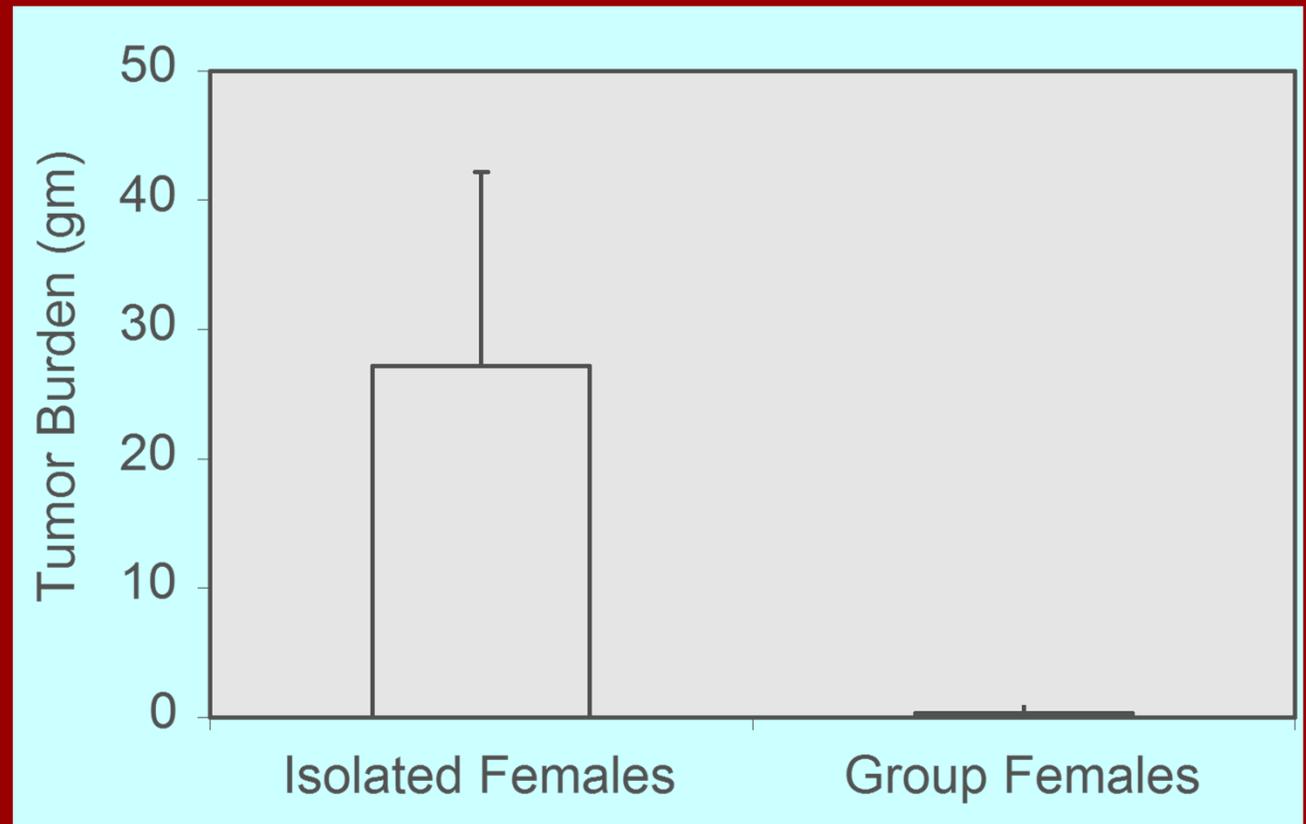


**Grouped**



**Isolated**

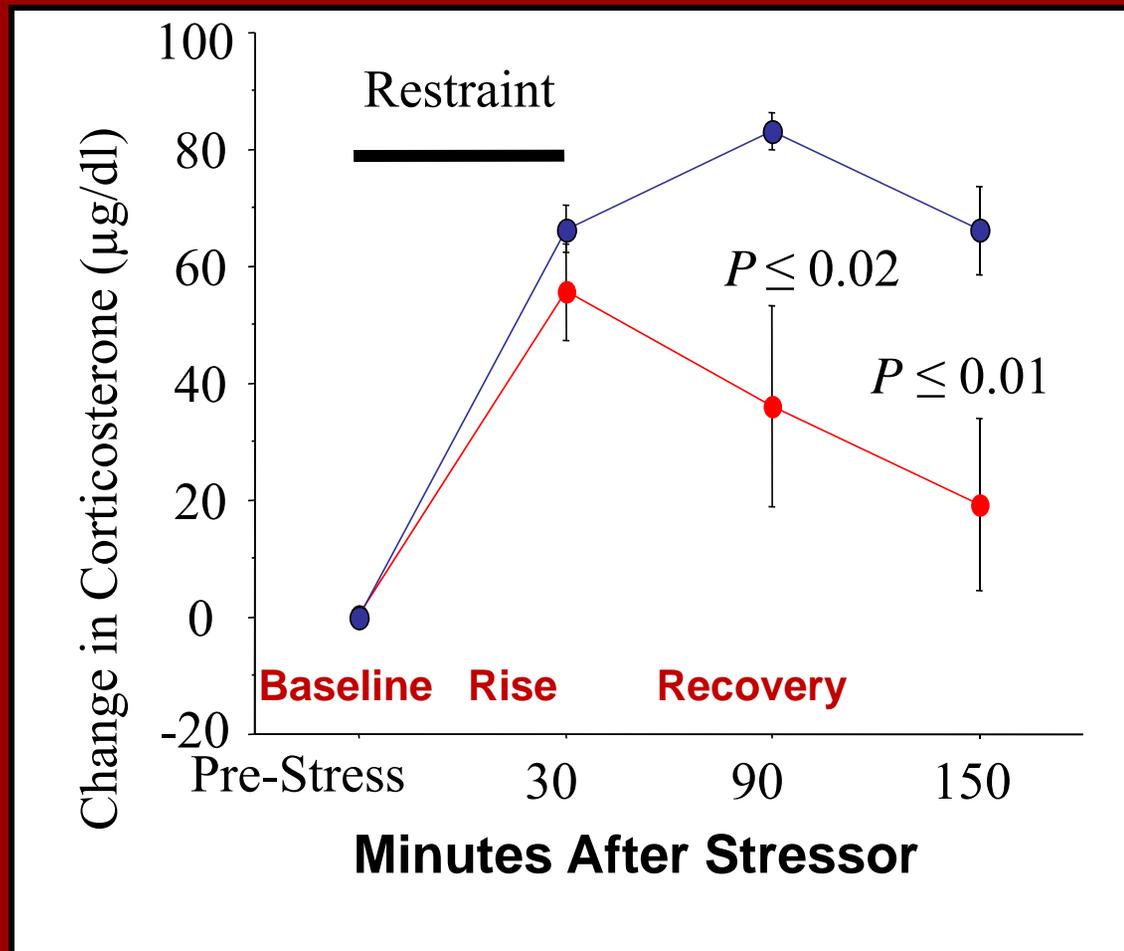
**Litter mates at 26 months**



$p \leq 0.0001$

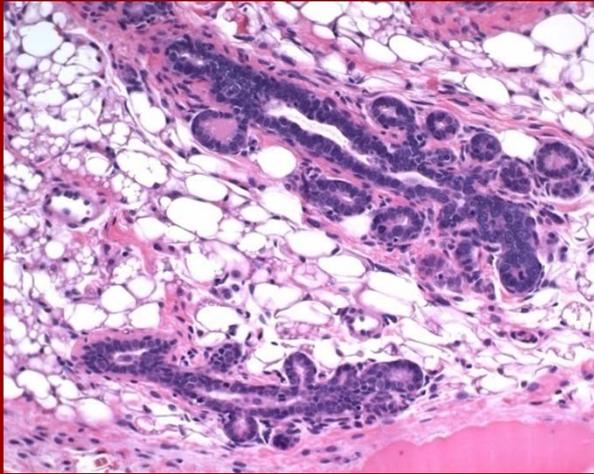
# Corticosterone Dynamics at 15 Months

## Endocrine Stress Response at Age 15 Months

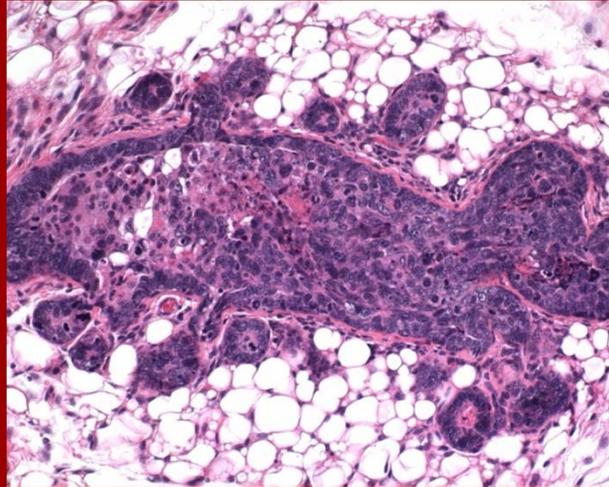


● Group ● Isolated

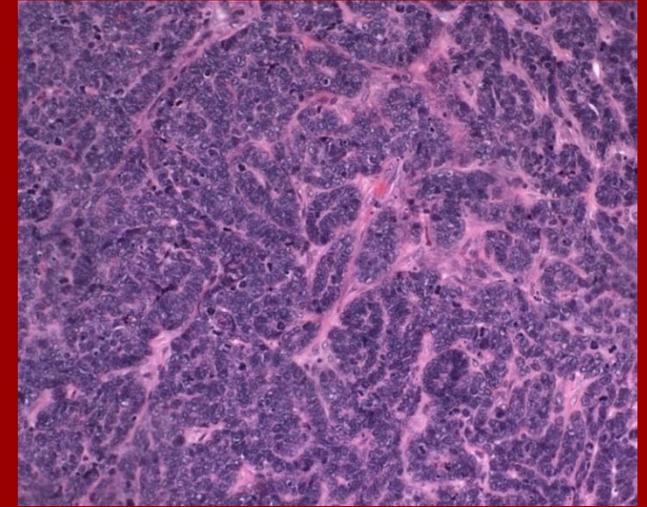
# GR Expression in Normal, CIS, and Invasive Carcinoma (SV40 mice)



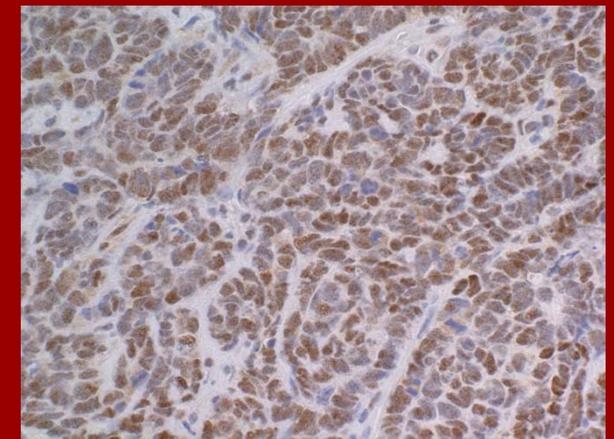
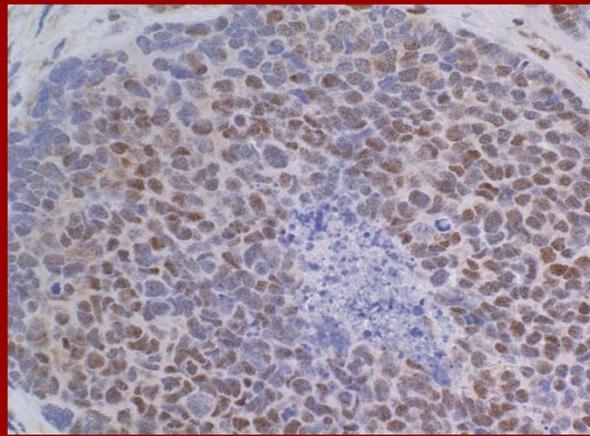
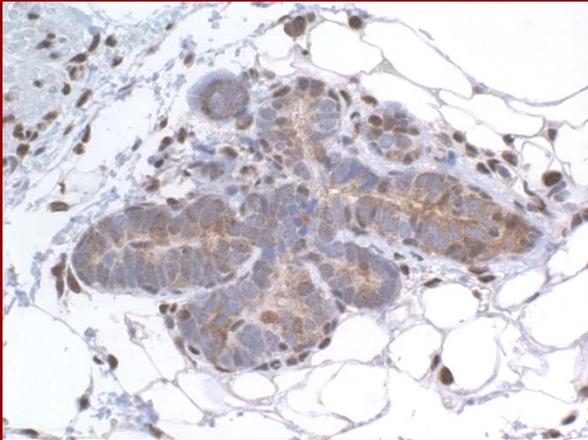
normal



*in situ*



invasive



Also, as tumors become more invasive, ER and PR ↓

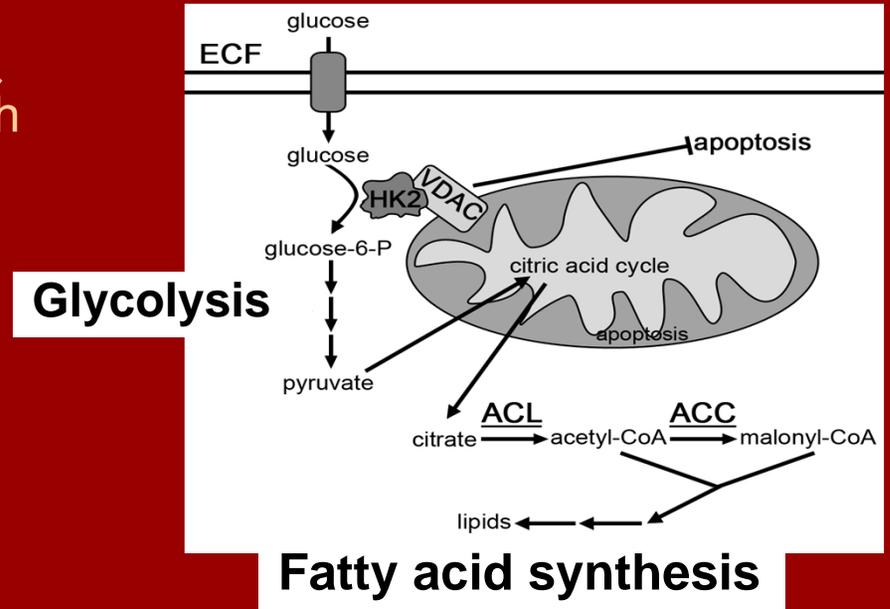
Courtesy of Conzen

# Metabolic Genes are Upregulated in Isolated versus Group Housed Premalignant Mammary Glands (MG)

Isolation → upregulated fatty acid synthesis & glycolytic pathway MG gene expression, which contribute to breast cancer growth

Isolated mice developed a heightened corticosterone stress response compared to group-housed mice

Suggests potential interventions, molecular biomarkers and/or targets (e.g., fatty acid synthesis) for prevention

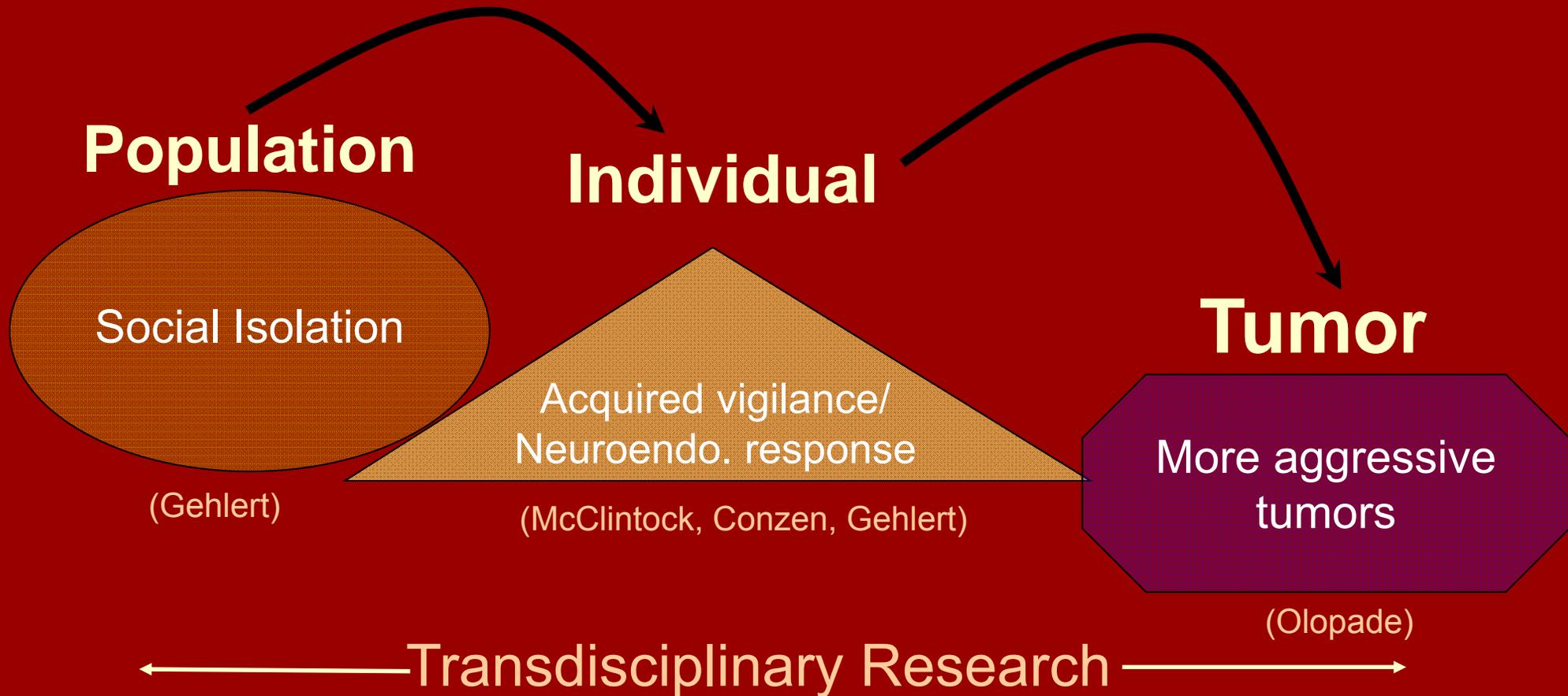


Williams et al., submitted

## Lessons Learned From Animal Work

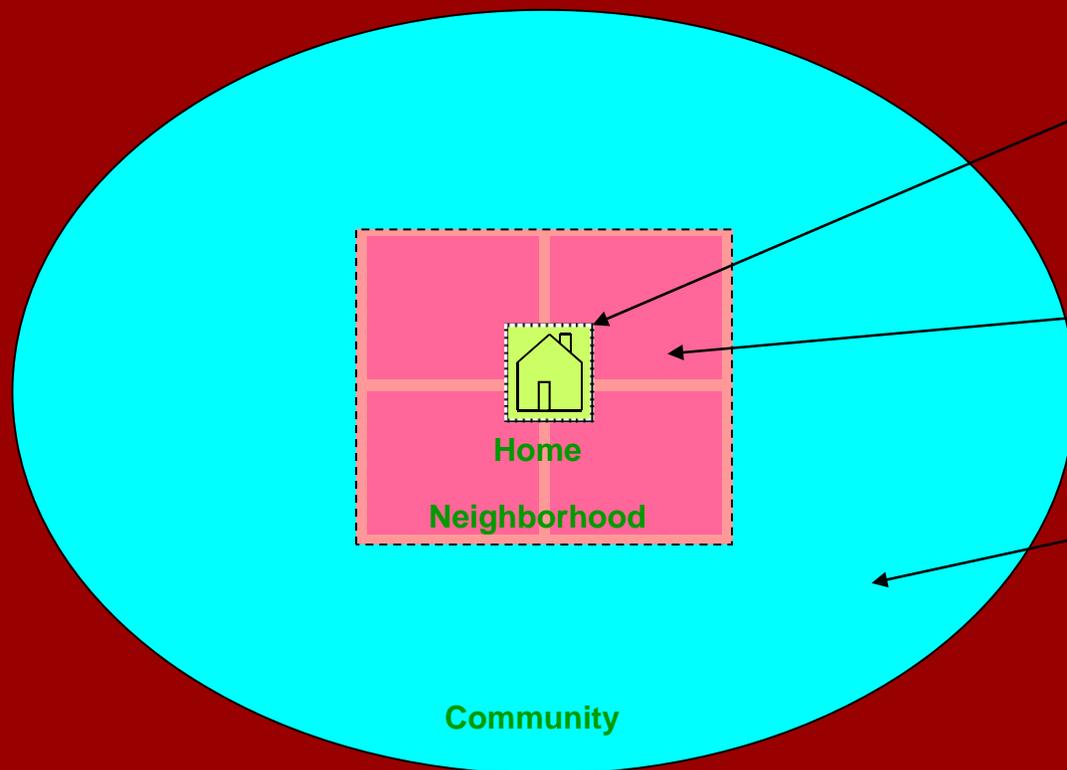
Endocrine stress response should be considered in understanding the biology of health disparities (hormone response is a conduit from social environmental stressors to gene expression)

# How Does Social Environment Affect Tumor Growth?



# Multi-Level Sources of Psychosocial and Hormonal Data from the Same Newly Diagnosed Women

Two-day visits every 6 months for 1.5 years (10 visits/woman with >18 hours of face-to-face contact).



**Home:** (interview in home) psychosocial functioning, social network, health behaviors, perceived discrimination, daily (4X) salivary cortisol.

**Neighborhood:** (four block radius around home; Built Environment Team) opportunities for social interaction (vacant lots, traffic in neighborhood, vacant buildings).

**Community:** (geocoded data) violent crime, collective efficacy, dilapidation of housing, SES, trust, health indicators.

Olopade lab collects and analyses tumors from same women

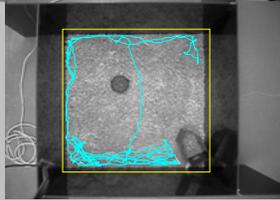
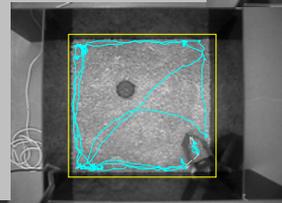
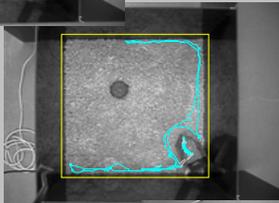
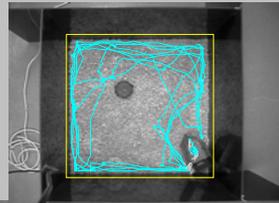
# Acquired Vigilance in Environment



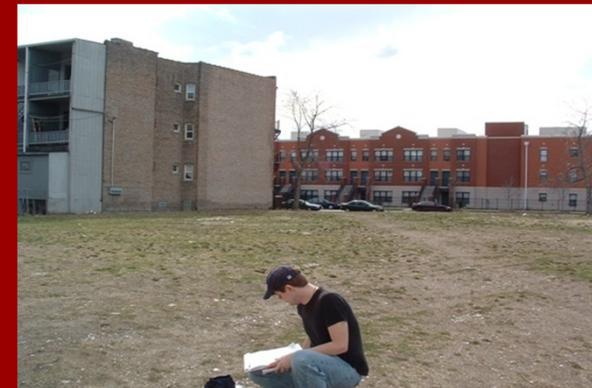
Isolated



Grouped



## Neighborhood's Built Environment



# Diurnal Salivary Cortisol Patterns Based on Cluster Analysis

## Legend:

Blue = Flat  
Green = Endocrine burnout



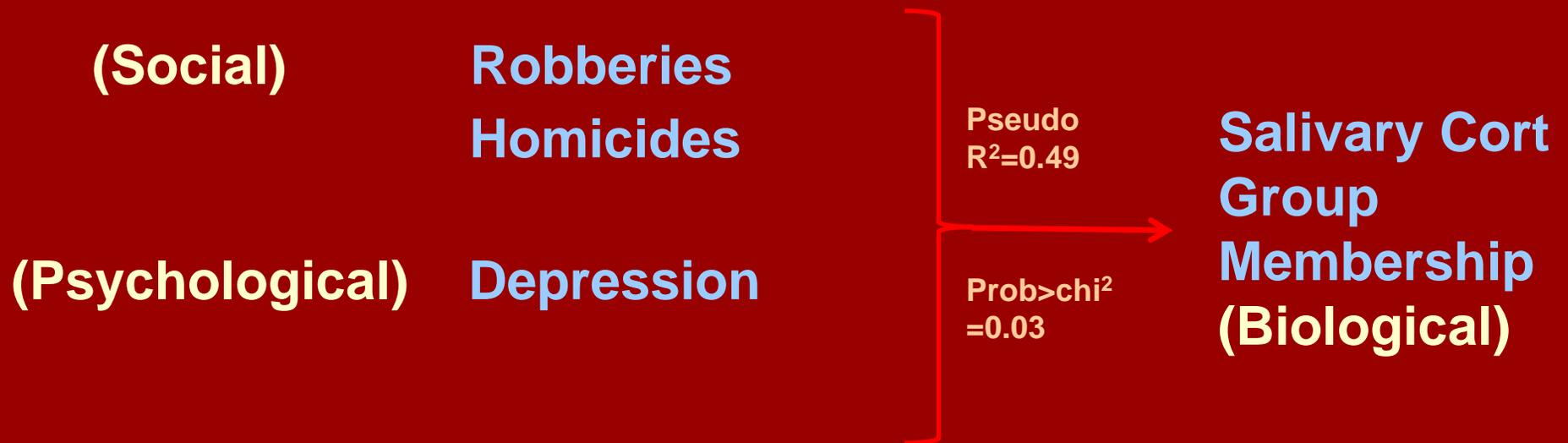
Measurement Time

## Lessons Learned

Cortisol rhythms are affected by neighborhood factors & psychological responses. Within-group variability in cortisol response that must be considered in designing interventions.

# Logistic Regression Predicting Diurnal Salivary Cortisol Group

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## Lessons Learned from Combined Animal and Human Work

Biological factors with clinical implications can be predicted from neighborhood factors. Targeting neighborhood factors with interventions is conservative of resources.



# Center for Interdisciplinary Health Disparities Research



Degraded  
Infrastructure

Crime

Unsafe  
Housing

Sexual Assault

+  
 $p = 0.00$



2-factor psychosocial suite:  
1. depression and loneliness  
2. anomie

+  
 $p = 0.01$

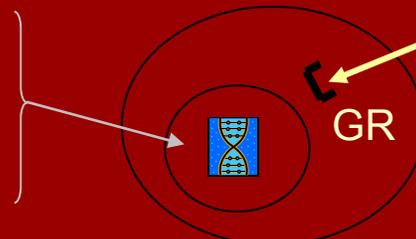
Inflammatory  
Process



Cortisol  
Dynamics

Nighttime Rise in Cort

Upregulation of Metabolic  
& Inflammatory Genes



GR

Glucocorticoid Receptors

# CIHDR Transdisciplinary, Translational Framework

CPHHD1

CPHHD2

Challenges

Products

Neighborhood  
(e.g. crime)

Shared model of  
white & African-  
American breast  
Cancer disparities

African-  
American  
women with  
mixed-SES  
Chicago

Transdisciplinary

Molecular  
(e.g. metabolic &  
inflammatory gene  
regulation)

Test  
Neighborhood  
Support  
Coordinator  
intervention

CER

Neighborhood  
intervention to  
improve clinical &  
biological outcomes

Test model with  
white & African  
American,  
impoverished,  
rural women

CER

CER

Advanced  
understanding of  
the roles of race,  
SES & geography  
in disparities

Build onto  
molecular  
pathways

CER

Targets for breast  
cancer prevention  
(e.g. fatty acid  
synthesis)